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论著

胃癌多药耐药细胞株BGC823/5-FU的建立及其耐药机制的研究

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摘要 目的：建立5-氟尿嘧啶（5-FU）诱导的胃癌多药耐药细胞株BGC823/5-FU，探讨凋亡相关蛋白Survivin、Bcl-2、Bax及caspase-3与其耐药性产生的关系。 方法:采用反复短期暴露并逐渐增加5-FU浓度的方法建立胃癌耐药细胞株BGC823/5-FU，MTT法检测此耐药细胞株对5-FU的耐药倍数及其对临床常用化疗药物阿霉素、丝裂霉素和顺铂的交叉耐药性，流式细胞术检测细胞P-糖蛋白的表达和柔红霉素积累量；Western blotting法检测耐药胃癌细胞株BGC823/5-FU与其亲代药物敏感胃癌细胞株BGC823凋亡相关蛋白Survivin、Bcl-2、Bax及caspase-3的表达。 结果:成功诱导出胃癌多药耐药细胞株BGC823/5-FU，较其亲代细胞BGC823对5-FU、阿霉素、丝裂霉素和顺铂的耐药性分别提高10.82、2.50、22.23和2.00倍。其P-糖蛋白表达较BGC823细胞增高（P<0.01），柔红霉素积累量较BGC823细胞减低（P<0.01）。与亲代药物敏感BGC823细胞相比，耐药细胞株BGC823/5-FU细胞Survivin表达上升（P<0.05），Bcl-2表达升高（P<0.05），Bax表达下降（P<0.05），caspase-3表达减低（P<0.05）。结论:胃癌细胞株BGC823在5-FU的诱导下可形成多药耐药细胞株BGC823/5-FU，P-糖蛋白、凋亡相关蛋白Survivin、Bcl-2、Bax及caspase-3可能参与其耐药性的形成。

关键词 胃肿瘤； 氟尿嘧啶； 抗药性,多药； 细胞凋亡

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Establishment of gastric cancerous multi-drug resistance cell stain BGC823/5-FU and its resistance mechanism

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Abstract

<FONT face=Verdana>AIM: To establish the gastric cancerous multidrug resistance cell stain BGC823/5-FU and investigate the relationship between the resistance and the expression of apoptosis related protein Survivin, Bcl-2, Bax and caspase-3. METHODS: Human gastric cancer cell line BGC823 was induced into MDR cell line by intermittent administration of high dose of 5-FU. MTT assay was used to detect the sensitivity of these MDR cells to some chemotherapeutic agents. Flow cytometry was used to detect the expression of P-glucoprotein and the accumulative value of intracellular daunorubicin (DNR) in these MDR cells. Western blotting was used to detect the expression of Survivin, Bcl-2, Bax and caspase-3. RESULTS: The resistance cell stain BGC823/5-FU was established, which possessed the ability of 10.82 fold resistance to 5-FU and cross-resistance to adriamycin, mitomycin C and cisplatin. The expression of P-glucoprotein was higher in BGC823/5-FU cells than that in BGC823 cells, while the accumulative value of intracellular DNR was decreased in BGC823/5-FU cells. Compared with its parent cells, expressions of Bax and caspase-3 in BGC823/5-FU cells were significantly down-regulated, surviving and Bcl-2 were upregulated in BGC823/5-FU cells. CONCLUSION: Gastric cancer cell line BGC823 has been induced into MDR cell line BGC823/5-FU. P-glucoprotein, Survivin, Bcl-2/Bax ratio and caspase-3 may play an important role in MDR of BGC823/5-FU cells.</FONT>

Key words Stomach neoplasms Fluorouracil Drug resistance multiple Apoptosis

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